EXHIBIT E

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION
Master File No. 2:12-MD-02327
MDL No. 2327

JOSEPH R. GOODWIN
U.S. DISTRICT JUDGE

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION

THIS DOCUMENT RELATES TO ALL WAVE VI CASES:

DEPOSITION OF

RALPH ZIPPER, M.D.

Friday, October 27, 2017
12:17 p.m. - 2:57 p.m.

Hilton Melbourne Rialto Place
200 Rialto Place
Melbourne, Florida 31901-3092

Stenographically Reported By:
Lisa G. Smith, RMR

I mean specifically, what were you asked to offer opinions on pertaining to TVT-Secur?

A. I was asked to render an expert medical opinion on the TVT-Secur device. The request was not more detailed. The reason the request was not more detailed, that may be a question -- that is a question that would be better asked to those that hired me.

However, more likely than not, the request was made in that form, the form that it was made in because these opinions are done in a somewhat standard fashion.

Q. And you've got a 267-page report that you've generated on TVT-Secur, correct?

A. Correct.

Q. And we're going to mark it in a second. Is it fair to say that all of the opinions that you would ever offer at trial pertaining to the TVT-Secur device are contained within these 267 pages of your report?

MR. THORNBURGH: Objection.

A. No.

BY MR. WALKER:

Q. And so what opinions pertaining to TVT-Secur are not contained within this report that you would offer at trial?

A. Can you please read back his question before

that question?

(The questions and answer starting on page 10, lines 15 through 24 were read back.)

A. So your first question asked if all the opinions I will offer at trial are contained in the report that you have in front of me. I do not know when the trial will be. If the trial was today, then all my opinions would be in that report or would be additional opinions that we would be -- come up in today's discussion based upon new things I may have read since the time of that report.

But let's say by way of example the trial takes place in a year. Over the course of the next year, I may read new articles. I may read additional expert opinions. Every time --

BY MR. WALKER:

Q. Sure, that's fair.

A. Please let me finish talking. You asked a question, please let me finish the answer and just as when you're asking a question, I won't interrupt you.

So when -- if I am exposed to new reports from the Defense, from the Ethicon experts, not only do I read those reports, I'll read the citations and references in those reports which may cause my opinion to be in excess of what you have in front of you today.

will be successful, and so TVT -- the efficacy was more than one percent. So there were patients that had good results from TVT-S.

BY MR. WALKER:

Q. Do you -- let me just back up a little bit. You treat patients for stress urinary incontinence currently, is that correct?

A. Yes.

Q. And what surgical procedures do you perform to treat stress urinary incontinence?

A. After I provide my patients with all the information necessary for them to make an intelligent informed decision, I perform the surgery that my patient has requested. The surgery that my patient has determined that the benefits for them as an individual will outweigh the risks and so whatever surgery I perform is based on the patient's informed decision. That can be anything from referring the patient out for physical therapy, to a transurethral bulking agent therapy to a traditional fascia lata sling to a full-length retropubic midurethral sling.

Q. I'm just asking you though if you could just list for me the different surgical options you provide your patients for treating stress urinary incontinence. You mentioned the retropubic synthetic slings. Are

there any others that you perform?

MR. THORNBURGH: Objection.

THE WITNESS: Lisa, can you please read back my answer?

BY MR. WALKER:

Q. Your answer involved non-surgical treatment options for stress urinary incontinence. I'm just trying to establish, Doctor, a list of strictly the surgical options that you provide your patients with.

A. Well, if Lisa read back my answer, you would --

MR. THORNBURGH: That's a different question than was originally asked.

A. However, I offer my patients procedural options that include transurethral bulking agent implantation, that include the sling surgeries, midurethral sling surgeries performed with synthetic material, as well as natural materials such as xenograft, allograft and autograft surgery.

BY MR. WALKER:

Q. What synthetic materials do you use when you surgically treat stress urinary incontinence?

MR. THORNBURGH: Objection.

A. I presently in a select group of patients, a small select group of patients, will offer them a

polypropylene mesh full-length midurethral sling.
BY MR. WALKER:
Q. And what product?
A. Whatever midurethral sling the surgical center or hospital has.
Q. Would that include the TVT retropubic full-length sling?
A. No.
Q. Are you able to recall any specific manufacturer that your facility provides?
A. Supplies have changed recently, but there was a time before I learned through the suffering injury of my patients and the chagrin of my peers of the complications that are associated with slings and therefore, as I did, I informed my patients. Less and less patients wanted slings.
So at one point in my career, I was doing well over a hundred slings a year. Maybe at this point I'm doing five or 10. Over the last year or two, those slings may have been manufactured by companies such as American Medical Systems and Boston Scientific.
Q. Doctor, would you agree that if you are providing as a treatment option a retropubic full-length synthetic sling, that it is within the standard of care to treat a patient for stress urinary

incontinence with that device?

MR. THORNBURGH: Objection.

A. I think it's a bit dangerous and confusing to apply the trade rubric standard of care to this situation and what a similarly experienced surgeon would do. I think the way to describe the implantation by me of a full-length polypropylene mesh sling at this point would be to say that it is -- it can be efficacious, it is efficacious.

However, the implantation is based on a risk benefit analysis and therefore, I need to spend a fair amount of time with patients informing them of those things that years ago we didn't know about about this product and then ask the patient to consider that benefit risk analysis and make a decision based on the new information we have.

Most of my patients will not want -- do not want and do not get a full-length retropubic sling, but there is a small subset of patients where to that patient, the risk benefit analysis results in that patient determining that they would like to have a full-length midurethral sling -- polypropylene mesh midurethral sling placed and I don't think standard of care is an appropriate description.

BY MR. WALKER:

Q. But you would agree that you're not operating outside of the standard of care when in your hands you implant one of these synthetic slings in your patients?

A. I would agree I am not doing anything unethical. I would agree that I am providing a full, informed -- I am fully informing my patient and helping them make the decision. I would agree that I am implanting the device in accordance with its regulatory clearance for the treatment of stress urinary incontinence.

If we were going to talk about a standard of care, this particular standard of care is -- it's a moving target. It's changing as we sit here as more and more specialists are recognizing that traditional full-length slings, not -- are recognizing the fact that traditional full-length slings are as efficacious as synthetic slings, although there is variable low-level data that suggests that short-term adverse events such as lower urinary tract symptoms and bleeding may be higher with traditional slings.

However, the re-analysis by my peers at this point is taking into consideration the fact that the data on those traditional slings did not put those slings at the midurethra and put them under tension.

And so the standard of care is slowly beginning to shift back towards traditional slings recognizing they were as efficacious and are as efficacious as synthetic midurethral slings and the potential downside of increased short-term lower urinary tract symptoms was because of the older method of implanting those natural slings.

So the standard of care is shifting and my comfort zone for answering your question is that I am doing something ethical for my patient based on that patient's risk benefit analysis.

Q. Doctor, would you ever implant any of your patients with a device that you believe was defectively designed?

MR. THORNBURGH: Objection.

A. To answer that with a yes or a no would paint a very grim picture of physicians overall because one needs to understand the implications of the defectiveness of the material and the defectiveness of the device and ultimately, that comes down to a risk benefit analysis.

The material is absolutely defective, and then I explain it to my patient and I tell them what that means. What does -- in my opinion, based on my knowledge, training and experience, based on what I've

have learned, what the manufacturers didn't tell me about the material, about how it behaves in the human body, what those material defects mean to that patient and for some patients, those material defects, the risks associated with those material defects are acceptable based upon the benefit.

A patient who is an extreme athlete who has failed other forms of management for incontinence, they've failed physical therapy, the patient has failed bulking agent therapy and it's dramatically affecting her life, and that patient does not want me to harvest their own tissue.

When I describe to that patient the material defects and they accept the material defects in this situation, I am willing to implant the material that has known material defects. But years ago, I couldn't have had that conversation with a patient because the device companies were not forthcoming about the material defects of their product. The patient could not make an informed decision.

Now, the patient can make an informed decision. There are situations where I will implant the product with a known material defect.

BY MR. WALKER:

Q. Do you believe that all polypropylene-based

mesh, cut the mesh. This is all part of the design of the material.

Q. Correct.

A. So would you -- is your question about the polypropylene molecule and the resin itself? Or is it about the way each individual manufacturer fabricates from that?

Q. The latter.

A. I am unaware of any fabrication of the polypropylene material, a material which is to this point universally defective when implanted in the female pelvis, I am unaware of any design using that material that negates the defective properties.

Q. Are you familiar with the proprietary additives that --

A. Are you talking about antioxidants?

Q. Will you let me finish my question?

A. Yes. I apologize. I did not mean to interrupt you.

Q. Thank you. Are you familiar with the proprietary additives that Ethicon adds to polypropylene to render the prolene material?

MR. THORNBURGH: Objection.

A. I recall reading a very comprehensive report by a company hired by Ethicon known as Exponent to look

at their polypropylene mesh and the end results of the process you're describing. So though I could not describe to you the antioxidant material used to inhibit degradation in the TVT-S sling, I have had the opportunity to look at the end result.

BY MR. WALKER:

Q. Would you agree with me that the mesh material of TVT-Secur is the same mesh material that's used in TVT retropubic and the TVT-O with the exception perhaps of how it's cut?

MR. THORNBURGH: Objection. I think it's a significant exception.

THE WITNESS: Could you please read back the question?

(The question on page 32, line 7, was read back.)

A. With the exception of how it's cut, with the exception of how it is shaped, and with the exception of the pieces that are added to it, it is my understanding that the base material, polypropylene is the same.

BY MR. WALKER:

Q. My question is a little more specific. The mesh itself, the weave of the mesh, the mesh material, would you agree that it's the same in all three

products?

MR. THORNBURGH: Objection, asked and answered.

A. When you originally asked the question, you attached it to an exception and so my answer provided that there are additional exceptions, and so you excepted the fact that it was cut differently and I want everyone who might read this transcript to understand that there are other exceptions that need to be considered as well.

But once again, if you're asking about the substrate and the resin and the polypropylene fiber that is extruded, it is my understanding that they're the same.

BY MR. WALKER:

Q. Let me try it this way: Would you agree that the pore size of the TVT-Secur mesh is the same as the pore size of the TVT retropubic and TVT-O?

A. I would -- it is my understanding that even scientists within Ethicon could not confidently agree with that because uniformity of fabrication was compromised and pore size varied even in one sheet of material.

But it is my understanding that the fabrication process was the same and the resin was the

same and the extruding fiber was the same, so there'd be variation, but that variation would most likely exist within each product type uniformly.

Q. I'm going to mark as Exhibit 7 Dan's favorite document.

MR. THORNBURGH: Objection.

BY MR. WALKER:

Q. This is the -- Doctor, I've handed you the AUGS SUFU's physician statement from 2016. You've seen this before, correct?

A. I haven't had a chance to review this in a while, so I may need a few minutes to look at it.

Q. If you'd like to take a few minutes, we can go off the record.

A. I'm unwilling to go off the record. I will do my best to answer your question, but to the extent that the question will require me to review this document which I have not looked at in a while, you could offer me the opportunity not to answer the question or please allow me to review the document, but it's -- there's only a limited amount of time, so let's start with the question, if you don't mind.

Q. The question is you've reviewed this document before, correct?

A. Yes.

discuss a single incision sling device that you worked on, is that correct?

A. Yes.

Q. Can you tell me what that device was and what your role was in the design or development of that device?

A. No. Just kidding.

Q. This is an easy question.

A. Jordan's like, come on, Ralph, please.

Q. Dude, I'm giving you a softball here.

A. Let the record reflect that this is a softball. Sure. In or about 2001, Dr. James Browning, a gynecologist from the other side of the pond, the UK, invented the single incision sling and he submitted that to the patent office and in 2003, Dr. Browning's invention to be commercialized through two companies in the UK and Scotland, Gyne-Ideas, G-y-n-e dash Ideas, and Mpathy, M-p-a-t-h-y, would receive a 510(k) clearance in 2003 and try to market that single incision sling in the United States. The world's first single incision sling.

And one of the first companies, if not the first company that Gyne-Ideas and Mpathy approached was Bard Urologic and in that time frame, I was doing a fair amount of consulting work for Bard Urologic,

hundreds of doctors were sent by Bard Urologic to Melbourne to go to my operating room and watch surgeries.

And when Dr. Browning approached Bard with his single incision sling and asked Bard to consider the purchase of the single incision sling intellectual property and perhaps the manufacturing as well, Bard suggested to Gyne-Ideas and Mpathy and Dr. Browning that they hire Dr. Ralph Zipper, yours truly, to evaluate the product, write a report and then have Mpathy in turn submit that report to Bard Urologic, who would then consider whether it'd like to go into a no-shop agreement and continue its due diligence.

I performed a series of surgeries using the world's first single incision sling invented by Dr. James Browning cleared by the FDA I believe in 2003 and memorialized my findings in a report which I submitted to Gyne-Ideas, Mpathy and James Browning and it is my understanding that based on my findings memorialized in that report that Bard opted to pass up the purchase of that intellectual property.

Thereafter, Gyne-Ideas and Mpathy continued to shop that single incision sling to multiple device companies in the United States. My recollection, that Boston Scientific was one of them. I don't recall

whether J&J and Ethicon was one of them, but they were unable to sell that single incision sling which had a efficacy of around 60 percent.

They were unable to sell that intellectual property in the United States and after they struggled for many years, I approached them and asked them if they would like -- if they were done trying to commercialize a product that had unacceptable low efficacy, the single incision sling.

By that point, Dr. Browning had been granted his patent and Dr. Browning and his companies asked me what I had in mind and I said you can't sell a 60 percent efficacy sling, we'll have to improve efficacy and you'll have to come to the United States and I'll have to help you do that and build sales behind it and then somebody will buy you.

And that's exactly what happened. It was a bit of a circuitous route. It was my assessment that a single incision sling could never be efficacious unless it was hybridized to become at least a temporary full-length sling with stabilization either at the level of the rectus fascia or the skin.

By hybridizing it and making it essentially no longer a single incision sling, it became a single incision sling slash percutaneous sling. I was able to

achieve efficacy that appeared to be at least as good as the full-length retropubic sling with adjustability and that embodiment of that improvement of mine created with my engineer would eventually be commercialized by Mpathy, U.S. in 2008.

Q. Is that device still on the market?

A. We'd have to go to the Coloplast -- the Mpathy product based upon my work product was first commercialized by Mpathy and then they exited to Coloplast. Coloplast purchased out and then started to sell it. It was certainly on their website for some time, a few years. I do not know if they're still selling it.

Q. What was the length of that sling?

MR. THORNBURGH: Objection.

A. I don't recall.

BY MR. WALKER:

Q. What's your best recollection?

A. I do not want to guess.

Q. Was it a full-length sling or a mini-sling?

MR. THORNBURGH: Objection.

A. Well, we can ask Lisa to read back. I've answered that. I described how the sling -- what the sling was, how it was a hybrid sling, why it was a hybrid sling, what defined it as a hybrid sling. So

the answer has already been given.
BY MR. WALKER:
Q. I'm really not trying to play games.
A. Jordan, neither am I. But by asking the same question three different times in slightly different ways, there's always the risk that I will answer slightly differently based on the way --
MR. THORNBURGH: Maybe a good question is what do you mean by hybridized?
BY MR. WALKER:
Q. Let's try that. What do you mean by hybridized?
A. As I had explained previously, based on my initial evaluation of the Mpathy single incision sling, a sling that had an anchor almost identical to the TVT-X, which was the first design of the TVT-Secur product which failed at least 40 percent of the time, and several embodiments of that failing sling that no single incision -- and it was unlikely a single incision sling would work unless it was at least temporarily a full-length sling. It was hybridized.
And so to hybridize the shorter sling, a sling material which did not penetrate the rectus fascia or the obturator membrane, tissues that are capable or more capable of retaining a sling, an

extension of the short mini-sling was created with a suture. That suture was carried through the thicker membrane such as obturator membrane or the rectus fascia and brought out percutaneously through the skin and then stabilized on the skin with a proprietary bandage, which I did receive a patent for.

So it was a short sling. A short sling which in all embodiments was not long enough to be carried through the rectus fascia or the obturator membrane and it was extended by means of a temporary suture.

Q. What was the sling made of?

A. Polypropylene mesh.

Q. What was the pore size of that sling?

A. Although I do not recall the pore size because that was -- I have a good memory, but that was almost a decade ago. I do recall that it was fabricated of a mesh that was substantially lighter than mesh that was being commercialized at the time.

The thought process is that a smaller inoculum, a smaller dose of a noxious material, a smaller dose of polypropylene would create less adverse events, whereas the TVT-Secur I believe had an adverse event profile of 65 percent. 65 percent of patients experienced adverse events. The thought was that you may be able to dramatically decrease the adverse event

profile by lowering the dose of the inoculum.

Q. Did your sling have an absorbable component to it?

A. My sling?

Q. Yes.

A. The suture material was absorbable.

Q. Other than the suture material --

MR. THORNBURGH: Objection.

BY MR. WALKER:

Q. -- was there an absorbable component to the weave of the mesh itself?

A. You mean like Ultrapro?

Q. Yes.

A. No.

Q. What were the perceived benefits that the sling would have offered to patients?

MR. THORNBURGH: Objection.

A. Device companies promoting their products for the treatment of stress urinary incontinence in the form of polypropylene mesh slings had done a poor job teaching a reducible method of adjustability. A goal of the design was to allow a reproducible method of adjustability that could potentially improve efficacy and decrease the incidence of short-term lower urinary tract symptoms.

MR. THORNBURGH: Objection.

A. I have not had a chance in preparation for today's deposition to go back and review the systematic reviews of the literature on full-length retropubic slings, but to the best of my recollection, common numbers are one percent, two percent.

BY MR. WALKER:

Q. Can we agree that TVT-Secur was first commercialized in 2006?

A. Yes.

Q. And by 2006, would you agree that the risk of mesh erosion from a synthetic sling was commonly known within the pelvic floor medical community?

MR. THORNBURGH: Objection.

A. Would you please define what you mean by commonly known? Are you asking me if it was an accepted number or what was talked about in barrooms when surgeons were talking about it, what did they believe the erosion rate was?

The problem with erosion rates before they were studied more carefully and looked at in systematic reviews is they were heavily underreported. Surgeons were embarrassed of their erosion rates.

BY MR. WALKER:

Q. Move to strike as nonresponsive. The

question isn't about erosion rates. The question is was the risk of erosion irregardless of what the rate would be --

A. Oh, did doctors know that erosion could happen?

Q. Was it commonly known in the pelvic floor medical community by 2006 that erosion was a potential risk of a synthetic sling?

MR. THORNBURGH: Objection.

A. Many and perhaps even the majority of surgeons that were implanting mesh understood that an erosion -- let me rephrase that.

Many, if not the majority, of surgeons believed that a treatable erosion could occur following the implantation of polypropylene in the vagina.

BY MR. WALKER:

Q. In 2006?

MR. THORNBURGH: Objection.

A. Many, if not the majority of surgeons who were actively -- let me rephrase that. Many, if not the majority of surgeons who had already implanted a significant number of polypropylene mesh products into the vagina had learned many, if not the majority, on their own through their experience with adverse outcomes in their own patients that mesh extrusion was

a possibility.
BY MR. WALKER:
Q. Would you agree that by 2006, it was commonly known to pelvic floor surgeons that dyspareunia was a potential complication following a vaginal surgery?
MR. THORNBURGH: Objection.
A. Before 2006, in 2006 and around the time of 2006, vaginal surgeons understood and believed correctly that pain with intercourse, comma, treatable pain with intercourse, was a potential complication of native tissue vaginal surgeries.
However, those same surgeries most and more likely than not the majority of pelvic surgeons were not aware that the complications known to them for native tissue surgeries when those same complications occurred with mesh-related surgeries were different and that treatment was difficult, if not often impossible leading to chronic morbidity.
BY MR. WALKER:
Q. Doctor, would you agree that by 2006, the potential risk of pelvic pain following vaginal surgery was commonly known to a pelvic floor surgeon?
MR. THORNBURGH: Objection.
A. Before 2006, and in and around 2006, I believe that the majority of pelvic surgeons understood

that transient and treatable pelvic pain could occur with any type of surgery, but at that point had very little experience and therefore very little understanding of the fact that the use of polypropylene mesh in the vagina would create a very, very different complication of pelvic pain, which would often more than not not be treatable.

BY MR. WALKER:

Q. Let me back up. What's the correct name or term for the sling that you developed? Is it --

A. Well, James Browning invented the sling. I just improved it. Many people went on to call it a stabilized mini-sling.

Q. But Mpathy, was that name of the sling or the company?

A. Mpathy was the name of the company. His original product was called Mini Tape.

Q. Okay. Was erosion a potential complication that could result from the sling that you developed?

MR. THORNBURGH: Objection.

A. Erosion is a potential complication of a polypropylene mesh sling. I did not invent the polypropylene mesh sling nor the defective polypropylene material. I improved upon the method of Dr. Browning by creating a hybridization of his

BY MR. WALKER:

Q. Is dyspareunia a potential complication of the sling that you developed?

MR. THORNBURGH: Objection.

A. In 2006 and 2007 when I was working with Mpathy and Gyne-Ideas to improve on the efficacy of that defective mini-sling product, my understanding of dyspareunia associated with the slings at that time relied upon the information provided to me by medical device companies.

Myself, like the overwhelming majority of surgeons out in the real world in private practice that are neck deep in healing and treating patients don't have time to go into -- in detail into medical literature. We more often than not rely on one journal.

By way of example, OB-GYNs rely on the Green Journal, and to that extent, my understanding of dyspareunia relied heavily upon what was given to me by the purveyors of slings and that was that it was transient.

So I believed that any dyspareunia that would occur with the mini-sling that I was working to improve would be similar to that associated with other slings. And my understanding at that time in 2006 and 2007 was

an understanding based upon the information given to me predominantly by the device companies that transient -- some of them talked of transient pain with intercourse and some of them did not talk of pain with intercourse at all, but I understood that it was a -- transient dyspareunia was a possibility.

BY MR. WALKER:

Q. And would you agree that irrespective of intensity or duration, would you agree that dyspareunia is a potential complication following any vaginal surgery?

MR. THORNBURGH: Objection. That's another significant exception.

MR. WALKER: But a fair one.

MR. THORNBURGH: No, it's not.

A. No.

BY MR. WALKER:

Q. What vaginal surgery is immune from the potential risk of dyspareunia?

A. The treatment of a urethral caruncle.

Q. Any others?

A. Oh, I'll take -- I'll need a few moments to think about it, but I'm sure there are others.

Q. Are you aware of any surgical -- strike that. Are you aware of any surgery to treat stress urinary

incontinence that's performed vaginally that doesn't carry with it the potential risk of dyspareunia?

MR. THORNBURGH: Objection.

A. Are you talking about transient and treatable dyspareunia or chronic and untreatable dyspareunia?

BY MR. WALKER:

Q. I'll provide the qualifier I did earlier. Irrespective of duration or intensity --

MR. THORNBURGH: Significant exceptions.

BY MR. WALKER:

Q. Irrespective of intensity or duration, Doctor, I'm just asking about the potential risk itself.

A. If we exclude significant and important exceptions such as permanency and untreatability, vaginal surgeries, incontinence surgery is associated with the risk of dyspareunia.

Q. Have you ever implanted a TVT-Secur?

A. I refused.

Q. So the answer is no?

A. The answer is I refused based on the obvious defects which were known to me because of my early work with the mini-sling concept and when it was -- TVT-Secur was brought to me, it was obvious if there was any way to fix the TVT -- if there was any way to

Q. Doctor, you write in your report that you have explanted TVT-Secur slings from patients, correct?
A. Yes.
Q. Do you know how many TVT-Securs you've explanted?
A. No.
Q. Do you have a system by which you keep track of what type of slings you're taking out?
A. Not a tracking system, no.
Q. In your report and in this deposition, you've been critical of the use of the polypropylene product in the slings, is that fair to say?
MR. THORNBURGH: Objection.
A. I have an expert opinion on the use of polypropylene mesh as a transvaginal implant.
BY MR. WALKER:
Q. Are you aware, Doctor -- strike that. What would be a safer material to use? Strike that.
What would be a safer synthetic material to use in terms of slings designed to treat stress urinary incontinence?
MR. THORNBURGH: Objection.
A. By nature, we tend as a species to be lazy inventors and we attempt to more often than not improve on a broken material instead of abandoning that broken

material, and this is what we've seen in the device phase. Well, how can we make this defective, noxious, injurious material better? Rather than abandoning it all together.

And in those attempts to improve on it, the Ethicon internal documents opined -- demonstrate that the Ethicon leaders opined as did others and other companies and scientists that the answer to improving it would be to use less of it.

And we talked about this earlier, a smaller inoculum, a smaller dose of the noxious, injurious material, and it is possible that using smaller amounts of the noxious material with effective porosity, pores that remain larger than 1,000 microns under load may reduce complications.

But the real answer is not what synthetic material -- the answer to the question is what synthetic material might be better or safer, the answer is natural tissue, native tissue surgery is more likely than not safer and better in the long run, if not in the short run.

MR. THORNBURGH: Do you mind if we take a break?

(Recess in the proceedings from 1:52 p.m. to 2:00 p.m.)

BY MR. WALKER:

Q. Doctor, can we agree that there's no such thing as a risk-free surgery?

A. Yes. Jordan, yes.

Q. That's great. One word. I love it. Can we agree that all surgeries have a learning curve to them?

MR. THORNBURGH: Objection.

A. Everything we do in life has a learning curve. Sometimes a learning curve is acceptable and sometimes it's completely unacceptable.

BY MR. WALKER:

Q. Would you agree that there's some surgeries that are more technically challenging than other surgeries?

MR. THORNBURGH: Objection.

A. There are certain surgeries that are so challenging indeed they should never be performed.

BY MR. WALKER:

Q. So is the answer yes?

A. The answer is that some surgeries can be significantly more challenging than others.

Q. Does the fact that a surgery that involves a medical device that results -- let me strike that.

Does the fact that a complication occurs following a surgery that involves a medical device mean

A. No.
Q. You wanted to add something?
A. No, we're just --
MR. THORNBURGH: He's answering your question before you ask it.
THE WITNESS: Let the record reflect that we're all laughing and at least Jordan is smiling, if not laughing.
BY MR. WALKER:
Q. In your opinion, would TVT-Secur have been a defective product if it had been made of Ultrapro mesh?
A. Absolutely.
Q. Would you agree --
A. It may -- it more likely than not would have been associated with less long-term fibrosis and inflammation, but it still would have remained a defective product associated with low efficacy and high complications.
Q. Would you agree, Doctor, that had TVT-Secur been made of Ultrapro, that it would have still carried with it the risk of recurrence?
MR. THORNBURGH: Objection. All things -- everything else being equal? In other words --
MR. WALKER: Correct.

MR. THORNBURGH: -- not changing the size --

MR. WALKER: Correct.

MR. THORNBURGH: -- not changing the laser cutting --

MR. WALKER: Correct.

MR. THORNBURGH: Okay.

MR. WALKER: All things being equal.

MR. THORNBURGH: Except for the material.

MR. WALKER: Correct.

THE WITNESS: Can you please read back the improved question?

BY MR. WALKER:

Q. How about let me just restate it so we have it clean. All things being equal, if TVT-Secur had been made of Ultrapro instead of prolene mesh, do you believe that it would have been a safer product?

MR. THORNBURGH: Objection. Significant exceptions.

A. I believe, as did Ethicon, according to its internal documents related to other products such as its Prolift product, that the movement to the Ultrapro partially absorbable mesh had a substantial chance of reducing complications associated with fibrosis,

contraction and pain.

However, secondary to the large number of substantial device-related defects associated and design-related defects and procedural-defects associated with the TVT-Secur device, the substitution of the prolene mesh for the Ultrapro mesh in the TVT-Secur product would more likely than not -- this is a double negative, I apologize -- not create an improvement that would have resulted in acceptable efficacy or an acceptably low complication rate.

BY MR. WALKER:

Q. Do you agree that pelvic floor surgeons -- strike that. Do you agree that a reasonably prudent pelvic floor surgeon will endeavor to read the medical literature to stay current on risks, complications that can be associated with the surgeries that person performs?

MR. THORNBURGH: Objection.

A. In the timeline of natural history of the development of a proficient surgeon, there's a very special period of time dedicated to the education of the surgeon where time is set aside for reviewing the literature, time is set aside for hand holding by mentors known as professors and that's called medical school and residency. And during that time, we

short. The initial TVT-X sling was 12 centimeters compared to a 48-centimeter TVT.

Well, we know that scaring takes place around the sling. That's how you get durable fixation and we know that the amount of fixation is proportional to the amount of material of which the scar occurs around. So when you place an eight centimeter sling in, you need an even better fixation device, a better fixation mechanism, instead of no fixation mechanism.

So there's -- the length was most likely -- more likely than not defective. The fixation means was defective. The inserter was defective. The inserter was so defective that key opinion leader Dr. Jaime Sepulveda dedicated 16 of his 29 slide lecture just to talking about how to take out the darn inserter.

The laser cutting of the product was defective, and this is just not my opinion this is the opinion of some of the Ethicon's key opinion leaders including Dr. Newman. Dr. Newman opined that the stiff laser cut edges were responsible for vaginal pain and the high erosion rates.

There is additional discussion of design and method defects that is described in my written opinion. There are.

Q. Doctor, what if any experience do you have in

device labeling?

A. Early on -- in the middle of my career in or about 2006, 2007, I as a consultant began writing labeling for pelvic organ prolapse and mesh products and sling products, but more recently, have been intimately involved in the creation of the labels for both of my companies which are in the process of coming to market with two devices in the women's health space that already have 510(k) clearances, but we are submitting a sub Q application for both an IDE and randomized control trials for new indications for use and those applications are associated with new labels and I'm in the process of writing those labels.

Q. Doctor, what if any methodology did you use in rendering your warning and labeling opinions?

A. So my method, which improves as all things do over time, my method relies on the FDA guidance, which includes the Code of Federal Regulations, Part 801, the adjoining guidance G91-1, includes the ISO guidance, including 14 630.

So my method begins by I open up all those pages. I open up the FDA guidance, I opened up the ISO guidance. I apply that to the development of my label. That's where my minimum requirements begin.

But ultimately, when you're going to be

ISO documentation and then improve on that, get input from the real end users and make sure the labels are adequate to accomplish what a label needs to accomplish to inform users and patients and make sure the device can be used safely and effectively for its intended use.

Q. That methodology that you just described, do you use that methodology in your practice as a CEO executive board member of device manufacturing companies?

A. Absolutely.

Q. Doctor, do you have an opinion one way or the other whether or not a sutured device for treatment of stress urinary incontinence is a safer, more -- a safe alternative design?

A. Yeah, absolutely. I believe that there was a systematic review of the literature in 2009 and/or 2011 by the Cochrane Group that compared the efficacy of sutured-device type repairs such as the Burch procedure, conventional slings and midurethral slings and those systematic reviews found that all three procedures, the suture-device-type repair, the Burch repair, the traditional sling, and the synthetic midurethral sling all had similar efficacy, so they were all equally effective.

There was some -- what they call variable and low level evidence to suggest that the synthetic repair had less short-term urinary tract symptoms, but there was no evidence of any long-term benefit from any one of those procedures over the other. So in the long term, the suture-device repair and the classical natural tissue sling repairs were equally effective and more likely than not safer.

Q. Doctor, do you have an opinion whether or not a full-length midurethral sling mechanically cut using Ultrapro would have been a safer alternative design than the TVT-Secur device?

A. It would have been safer.

Q. As a CEO or an executive and board member of medical device manufacturing companies, do you have an opinion one way or the other whether or not Ethicon and Johnson & Johnson acted as a prudent manufacturer could have acted in manufacturing, designing, selling and labeling the TVT-Secur device?

A. Yes, I do.

Q. What's that opinion?

A. My opinion is that Ethicon slash Johnson & Johnson took unacceptable shortcuts and thereby failing to provide safety and efficacy for the devices subject to today's deposition, the TVT-Secur device.

CERTIFICATE OF REPORTER

THE STATE OF FLORIDA)
COUNTY OF ORANGE)

I, LISA G. SMITH, Registered Merit Reporter, certify that I was authorized to and did stenographically report the foregoing deposition of RALPH ZIPPER, M.D., pages 1 through 99; that a review of the transcript was requested; and that the transcript is a true and complete record of my stenographic notes.

I further certify that I am not a relative, employee, attorney, or counsel of any of the parties, nor am I a relative or employee of any of the parties' attorney or counsel connected with the action, nor am I financially interested in the action.

DATED this 7th of November, 2017.

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Lisa G. Smith, RMR